

## Chapter 1

# Introduction

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Neural tube defects (NTD) are the most common disabling congenital malformations. Three hundred thousand individuals are born each year with NTD. It is safe to state that every pediatrician will be involved in the care of children with NTD more often than children with brain tumor.

The neural tube is the primordial structure of the central nervous system. The brain and the spinal cord will develop from the neural tube, guided by a delicate and ill-defined interaction between genes and the environment. This process transforms a flat slab of tissue, the neuroectoderm, into a hollow structure that at one stage stretches along the full length of the embryo. Eventually the neural tube will fade after it is completed.

At term the brain and the spinal cord will be fully formed while none of the original components of the neural tube is identifiable in the newborn. This is true for most people, except for a small but persistent number of individuals (year after year, since the dawn of recorded history), who will carry an anatomical anomaly resulting from an imperfect closure of their neural tubes.

A neural tube is defective when it fails to close between 18 and 28 days following conception. The problem can be anywhere along its structure and according to the location of the opening, the child will have one of a gamut of pathologies that ranges from simple to fatal, from spina bifida to anencephaly, from mild to severe. As the defect happens in a short but crucial moment of development, some patients will have different associated anomalies and others will not, thus highlighting the protean manifestations of NTD. The physician who has been told that a child with any of the NTD conditions will be transferred to his/her care has to be prepared for a few scenarios and leave space for the unexpected. Each patient with NTD is a unique clinical case that will capture the attention of an inquisitive physician.

The etiology or etiologies behind the development of NTD remain ill defined. Prevention through a daily dose of folic acid by the mother before conception has decreased its incidence substantially, but still it has not eradicated the condition. It is a mistake to presume that dietary supplementation of folic acid is enough to prevent this congenital anomaly.

In the developing countries, the incidence of children born with NTD is double or triple than the incidence in the industrialized nations. The difference in incidence also follows the pattern of the poverty line. In Guatemala, the incidence of NTD is 1.6 per 1000 live births; the only places where this figure is similar to the US are few hospitals in the privileged zones of Guatemala City. In contrast, the prevalence of NTD in Quiche, a rural and backward region of the country, is one of the highest in the world. And this difference in Guatemala cannot be attributed alone to prenatal diagnosis that leads to elective abortion.

Interestingly, there is also a different attitude towards the disease. In the US, which has prevalence below the world average, there is an effective healthcare facility available for taking care of children born with NTD. Conversely, more often than not, the parents of a child born with NTD in Guatemala or Kenya are told that their child's condition has a guarded prognosis and is tantamount to immediate demise. These beliefs have led to the accepted practice of sending the child home under the care of their parents, in a great number of nations. Finally when the child has tenaciously continued to live, the family will start a sort of "pilgrimage" between various medical centers that will exhaust their resources and stamina. Thus a child in a developing nation, who has survived the initial brunt of being born with NTD will continue to survive, plagued by preventable complications and thus will be unable to achieve his or her expected intellectual abilities. In Guatemala, 90% of children born with NTD die in the first five months of life. Even if only 10% of the untreated children survive, they represent an increasing number of population who have been virtually neglected by society. It is believed that in rural areas of developing countries, the mortality can reach 100%.

This clearly shows that depending on the location where such a child with NTD is born, its clinical outcome is apt to vary. The scenario in developed nations are different with tremendous resources being allocated to improvement of healthcare.

Furthermore, current US President Barrack Obama has raised the question on how much investment a nation can afford in improvement of healthcare. Following this argument, distinguished thinkers such as Peter Singer have advocated for a dispassionate definition of futility that necessary leads to asking the true worth of human life, the latter defined not by the needs of the individual but by the needs of the society that nestles him/her.

In March 2005, Drs Eduardo Verhagen and Pieter Sauer from the University Medical Center in Groningen, the Netherlands, published in the *New England Journal of Medicine* the protocol for neonatal euthanasia. They report that in a way neonatal euthanasia had been prevalent in their country for decades. By proposing a set of rules to be followed by physicians and parents, the authors acknowledge that the situation they are describing is more real than the society is ready to accept. The Groningen protocol focuses only on perceived or potential suffering by the newborn, it does not ever mention national economic resources as an argument for their position. Nonetheless, in an article in the *Los Angeles Times* in March 2006, Peter Singer linked neonatal euthanasia to the stress of healthcare budget by highlighting that infant mortality in the Netherlands was much less than in the US. Singer attributed this difference to the better management of resources in the US.

In any case, the set of instructions developed by European neonatologists remind us that the subjective perception that patients with disorders of the brain or the cord are less recoverable than any other patient is more prevalent than we want to admit.

As briefly mentioned above, elective abortion of the child with antenatal diagnosis of NTD could be a cause of the decrease in its prevalence in other nations. Jonathan Glover in "*Causing Death and Saving Lives*" reproduces a letter to the editor of *Times* from a parent of a child born with spina bifida. A part of the text reads, "Why can one kill perfectly well babies by abortion and yet if they are actually born (but turn out wrongly) insist they live, even to the extent of operations, incubators and oxygen tents?"

The reference to this debate is pertinent to this book because the great majority of euthanized neonates in the Netherlands had spina bifida. Any patient with NTD, either because of mental retardation or dependence to a wheelchair or a ventriculoperitoneal shunt for hydrocephalus, represents

one of the three groups of elective patients defined in the Groningen protocol: “infants with a hopeless prognosis who experience what parents and experts deem to be unbearable suffering”. The authors acknowledge that this group is difficult to define but serve us the example of “a child with the most serious form of spina bifida”.

For the moment, until the debate becomes part of public policy, it is patently clear that in the industrialized nations we still take a proactive position with our patients with NTD. We approach them with the same impetus as we do with other patients with cardiac or renal chronic disorders.

But it has to be acknowledged that while we may not be ready yet to let the budget rule the way we treat our patients, we have become accustomed to linking economy to healthcare needs, even if that is done bypassing human rights in the process.

The Western nations have been rightly protesting the lack of medical treatment for patients with AIDS in sub-Saharan Africa. Former South African President Thabo Mbeki has been ridiculed by his stance on the origin and treatment of AIDS. In contrast, the Western advocates for global health have not raised the issue of patients with NTD, perhaps because as mentioned above, we have accepted that in developing nations the needs of patients with NTD are prioritized according to the available budget.

Perhaps, when hearing of a developing nation, some readers may have a limited idea of what it means. The boundary between a country about which we are aware through the daily news because of deep unrest, and a country that while struggling against economical odds has not slid into chaos is not always well traced. To continue with the case of Guatemala, this is a nation with a gross national product of 48 billion US dollars. The nation is not prosperous by industrialized standards but neither has it sunk into an economical void. But still, only 10% of the children with NTD survive up to five months of age.

The current situation demands a solution and it could come by adopting one of the following three options:

1. Improve prevention and treatment of NTD.
2. Implement the Groningen Protocol for euthanasia of the severely ill newborns.
3. Continue the status quo.

The first alternative implies that physicians understand that their patients have similar chance of recovery and improvement as any other subgroup of pathologies. Patients who have cancer or chronic infectious disease will not fare better than patients with NTD if they are abandoned to their fate. A group of devoted physicians can start a spina bifida clinic. Eventually the project will grow. There are international NGO and healthcare agencies that can finance the project. The accumulated experience by a single group of physicians that follows patients whose defects were corrected at different stages of the patients' lives will provide valuable information about the natural history of NTD and its associated conditions.

There are two compelling arguments in favor of transforming NTD into a subject of interest for healthcare officials of a developing nation.

First, the number of working hours that the family spends every year by going back and forth between skeptic physicians of various specialties who cannot solve preventable complications are wasted time for the national economy. I have had the opportunity to participate in numerous clinical and surgical workshops in many countries and I have witnessed, and admired, the determination of the parents of children with NTD who persistently travel to the capital, attracted by the news of a team of foreign doctors laboring with their local colleagues. If the parents of a child with spina bifida from Guatemala feel that everything possible was done for their handicapped child they will carry on with their life and work with the same relief that any other parent from an industrialized nation will feel. The children with the disability will have limited educational opportunities and this will deepen their dependence and indirectly the dependence of their families.

Second, the equipment required for the majority of NTD reparative surgeries is not more sophisticated than the ones required for an abdominal surgery. More often than not, the elements for solving the problem are present but remain idle. Equipping a hospital and training doctors for addressing many NTD conditions in the newborn will improve the medical care of other conditions besides NTD.

The euthanasia of the newborn according to the Groningen Protocol will require a daunting effort from the physicians and the families, and even a debate in the legislative branch of government. The idea, to the best

of my understanding, is impracticable. There may be a group of parents who wish that their children were dead, and although I have seen many children with NTD who were abandoned by their families, all were left behind in places where they could be easily found and were swaddled in warm clothes.

Leaving things as they are will perpetuate a problem. And in essence this is a moral fallacy. Euthanasia is also performed by nature but not everybody dies. Eighty percent of the children born everyday do so in developing nations, where NTD have a higher incidence than in their industrialized counterparts. So while the government of a developing nation acknowledges the problem by enforcing fortification, it has been shown that the prevalence of NTD does not zero the incidence; while multiple issues regarding prevention are being implemented and perfected, children with NTD continue to be born. The problem is here today for 300,000 families every year.

Virchow declared that medicine is a social science, thus it is reasonable to infer that the physician is a social worker. This mantle does not cover only the general practitioner, or the public health official; it encompasses every physician who is devoted to treating complex diseases, independently of their prevalence.

The neurosurgeons, the geneticist and every one of the specialists who work with patients with NTD are immersed in the struggles of the society where they live, even if some presume that they are not. It goes without saying that patients, their families and their physicians are members of the same society. They all know that a newborn with neural tube defects represents a formidable challenge for the healthcare system of any nation. When basic care is provided the conditions are rarely fatal, therefore the shape and weight of the problems that the physicians will have to confront will vary according to regions of the world.

The truth is that in the great majority of the countries in the world, there are facilities for looking after a wide array of pathologies associated with NTD. I have visited and worked in public hospitals in nations from every continent and everywhere I found teams of physicians absolutely capable of tackling the most complex case of NTD.

It is even fair to state that the difference between developed and underdeveloped nation is less wide when we compare the quality of the

physicians at both sides of the divide. I have also witnessed that the enthusiasm of many is slashed every day by the realities of society. And here we return to the question indirectly posed by Virchow, is the physician an agent of social change?

Some authors believe that the doctor has to be devoted to his patient and not be preoccupied with philosophical activism, of which politics is one of its branches. Fair enough, so what can we do to face the challenges posed by our patients?

It has been estimated that the cost of treating a child with spina bifida is close to US\$350,000. The elements of this enormous expense are education and medical care. Certainly a child who never had an infection, only one shunt for hydrocephalus, and who had adequate care for urological and orthopedic complications will represent one end of the curve. The benefits of adequate treatment and prevention can be quantified in dollars. Let us reduce the suffering of each of our patients with the understanding that we will be improving the national healthcare budget — a proposition that seems inadequate for a physician, but it is the language that administrators and politicians understand and the benefit for all the patients will be immense. This can be achieved without surrendering any of our principles as physicians.

It is the purpose of this handbook to provide an encompassing review of the clinical aspects of all neural tube defects. The text is succinct but not basic and is centered on the clinical neurosciences because NTD is, above all, pathology of the central nervous system. The details of the different surgical techniques are mentioned to facilitate the understanding of the pathology.

When writing this book we had in mind the pediatrician and general practitioners who practice anywhere in the world and mostly from rural areas where patients with neural tube defects are born at a rapid pace every day.